Letter to the Editor

**Reply to Letter to the Editor: "Comparing milled fiber Quebec ore, and textile factory dust: Has another piee of the asbestos puzzle fallen into place?" by D. Wayne Berman**

by

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**Response to "Letter concerning "Comparing milled fiber, Quebec ore, and textile factory dust: Has another piece of the asbestos puzzle fallen into place?" by Berman" by Dement and Stayner (Accepted for publication in *Critical Reviews in Toxicology)***

I have carefully considered the thoughtful comments provided by Drs. Dement and Stayner regarding my article (Berman 2010) and provide responses in the following text. Each of my responses is preceded by the quoted comment.

1. **Sentence beginning on Line 8 of the first paragraph (Page 1): "...we do not agree with Dr. Berman's analyses of our TEM data for the Charleston, South Carolina asbestos textile plant to support his conclusion that airborne fiber size distributions within a give industrial sector (e.g., textiles, friction products, cement, etc.) vary little by operation."**

I would like first to emphasize that I did not conclude in the 2010 article that there was no difference in fiber sizes between operations (zones) at the South Carolina (SC) textile plant, only that such differences are relatively small, especially in comparison to temporal variation within the plant as a whole. The data presented in Figure 3 and Table 7 (of Berman 2010) demonstrate this and I also address this issue further (below). I would additionally like to suggest that, due to mismatches in the collection dates for samples from different zones, pooling samples may not entirely cancel effects due to temporal variation and this may partially mask true differences across zones. At the same time, because Dement, Stayner, and coworkers generated only single size distributions for each zone (by pooling the data), they were not able to evaluate the effects of temporal variation; the simulation they conducted addresses uncertainty but not variation (Dement et al. 2008, Stayner et al. 2008).

To further illustrate that differences in sizes between zones of the SC plant are small, see attached Table 1. This table was derived from Table 4 of Dement et al. (2008) simply by (1) summing across widths within lengths (top of table) or lengths within widths (bottom); (2) summing over lengths (or widths) within zones; and (3) taking the quotient of the value for each individual length (or width) and the sum of these categories within each zone.

The top of Table 1 presents the relative fraction of fibers in each length category considered by Dement et al. (2008) for each of the zones of the SC plant along with the minimum, maximum, mean, and max/min ratio across zones. The bottom of the table presents similar information for the fraction of fibers in each width category. As can be seen in the table, the variation across zones for all but the largest two length categories is less than a factor of 2 and (when Zone 10 is excluded) is only greater than a factor of two for fibers longer than 40 μm. Of course, given that fibers with L>40 μm represent only 1% of the total number of fibers counted (and thus subject to less precision), it is not surprising that this category would exhibit somewhat greater variation. A similar pattern is observed for width; the narrowest category shows less than a factor of 2 variation across zones while (with Zone 10 omitted) the thicker zones (which respectively include only 10%, 3%, and 0.6% of the fibers) show small but somewhat greater variation. Moreover, visual inspection of the table shows no obvious or robust pattern of increasing or decreasing length (or width) as operations move from start to finish at the plant. Note, as mentioned in Berman (2010), it is not clear whether Zone 10 is more substantially different from the other zones or whether estimates from this zone are simply less certain as no structures were counted in this zone for 7 of the 20 size categories (including 6 of the 8 thickest categories) tracked by Dement et al. Note also that temporal variation observed across SC samples is substantially larger than a factor of 2 (Berman 2010, Figure 3).

2. **Sentence beginning on Line 12 of the first paragraph (Page 1): "We believe this conclusion is not consistent with known effects of asbestos textile production operations, is not supported by prior studies, and is not consistent with results of studies of asbestos textile mills in South Carolina and North Carolina." and second paragraph, beginning on Line 18 (Page 1): "A review of asbestos textile processes would not lead one to conclude that airborne fiber characteristics would be the same across departments........"**

I believe my results are consistent with the known (or suspected) effects of production operations. Because bulk materials are "classified" (separated by size with shorter fibers and grit being removed from the material passed on for later processing) during bulk preparation and, potentially, carding, it is possible that the size distributions of airborne dusts in these two operations contain a larger fraction of shorter fibers and non-fibrous dusts than dusts associated with downstream operations in a textile plant. Results from Lynch and Ayer (1966) also suggest that this is true (see Response No. 4 below). Interestingly, results from Dement et al. (2008) appear to contrast with such observations (Response No.4 below), although this may simply be an artifact due to masking by larger sources of variation; my analysis of both the SC data (Response No. 1 above) and the data from Lynch and Ayer (Response No. 4 below), indicate that differences across operations are small relative to the magnitude of temporal variation.

Note that the latter clauses of the quoted comment from Line 12 (above) are explicitly addressed in the rest of my responses below.

3. **Third paragraph, beginning on Line 32 (Page 1): "Additionally, Dr. Berman's conclusion is not consistent with prior studies including the 1938 study of North Carolina asbestos textile plants (Dreesen et al. 1938). These authors commented on the highly variable gross and microscopic appearance of airborne dusts collected in the various textile departments......"**

I am not sure how best to address the comments concerning the Dreesen et al. (1938) study. The authors do not provide enough detail in their article to allow any reasonable evaluation of the fiber size data that they present (Table 6). For example, the article reports neither the number of fibers counted to derive the estimates of median length, nor the dimensional criteria used to define the nature of fibers included in the count. More importantly, they provide no information on the confidence that can be placed in the values reported. Thus, it is not even possible to determine whether the median lengths reported for the various operations are statistically distinct from one another. I simply suggest that, to the extent that the results of Dreesen et al. (1938) are consistent with the work of Lynch and Ayer (1966), which are addressed in Response No. 4 below, then they can be considered consistent with my findings as well. I would also like to emphasize that the question of the relative fraction of fibers in total dust was not addressed by the (TEM) size distributions reported in Berman (2010) that were compared to the SC data, so questions concerning the fraction of total dust represented by asbestos fibers are not directly relevant to this discourse.

4. **Fourth paragraph, beginning on Line 43 (Page 1): "Lynch and Ayer (1966) measured total fibers, fibers >5 µm, and fibers > 10 µm by phase contrast opical microscopy in U.S. asbestos mills and found the ratio of concentrations of fibers > 10 µm to total fibers progressively increase from preparation to weaving.......".**

It is clear from the attached Table 2 that the data presented in Lynch and Ayer (1966) suggest that, whatever differences may exist in size distributions between operations, they are small relative to differences observed across plants (which I believe are also likely to reflect temporal variation within plants). Thus, the findings of Lynch and Ayer appear to be entirely consistent with the findings in Berman (2010) and my responses above.

To develop Table 2, I took the data presented in Table III of Lynch and Ayer (1966) and calculated the ratios of fibers > 5 µm to "total" fibers (actual size range not stated by Lynch and Ayer) and of fibers >10 µm to total fibers as a function of both plant and operation. As can be seen in the top half of the table, the >5/total ratios (averaged across plants) for each operation are quite close while the range (minimum to maximum) of values observed across plants show very high overlap between operations in all cases. This indicates that the differences between operations are all small relative to the differences between plants (and, likely, the temporal variation within each plant). A similar conclusion is reached when the >10/total ratios are evaluated (bottom half of the table). Interestingly, though differences across operations are small, they do suggest (by an apparent trend) that fibers in dusts from preparation and carding may be shorter than those observed in other plant operations. However, such a trend is not apparent in the Dement et al. (2008) data from the South Carolina facility (last column of Table 2). Thus, either the Dement et al. data are inconsistent with the Lynch and Ayer data or (more likely) any real trends are simply masked by other sources of variation.

5. **Sentence beginning on Line 54 (Page 1): "Finally, Dr. Berman's analyses and results are not consistent with results of our studies of asbestos textile mills in South Carolina (the Charleston plant) and North Carolina....".**

I believe that the above four responses indicate that my results are consistent with the results of the various studies cited by Drs. Dement and Stayner in their letter. In contrast, if anything, it is the results presented by Dement et al. (2008) that may not be consistent with these other studies (see Response No. 4), although it is more likely that relevant trends may simply have been masked in the Dement et al. study. Also, see Response No. 9 below.

6. **First full paragraph, beginning on Line 16 (Page 2): "Dr. Berman performed a number of statistical analyses of the Charleston plant samples which violated our study design and draws into question validity of his analyses and conclusions. First, Dr. Berman attempted to calculate bivariate size**

**distributions for each of the 83 TEM samples. As discussed previously, our *a priori* study design required that individual samples within a department be combined in order to reasonably estimate the bivariate size distributions ......... We do not believe calculation of bivariate size distributions on these <u>individual</u> samples is a valid statistical exercise."**

It is true that Dement, Stayner, and coworkers saved money on their laboratory analyses of individual samples so that they were not as robust as might otherwise be the case. The consequence of this decision is simply that size distributions derived from their data for individual samples are of lower precision than might otherwise be desired.[1] But limited precision is a problem handled by interpreters of TEM data all the time (see, for example, Berman and Chatfield 1990). Importantly, their counting rules introduced no bias. As long as there is no bias in the counting rules, there is no reason why evaluation of size distributions developed for individual samples from their data should be considered invalid. Thus, I disagree with the notion that comparing data from individual samples in their data set is inappropriate. Other than stating that they chose to pool the data, Drs. Dement and Stayner provide no technical justification suggesting anything wrong with not pooling their data. One must simply be careful to adequately consider precision and the increased frequency of zero counts, both of which I addressed in my evaluation. Moreover, by adopting their study design, Dement, Stayner, and coworkers were *assuming* that any differences observed across operations would automatically be due to differences in the mechanical processes associated with each operation, rather than other causes (such as temporal variation, as stated in Dement et al. 2008), but their study design precludes the possibility of testing that assumption. In contrast, comparing size distributions from individual samples (as I did) allows formal testing of that (and other) assumptions.

7. **First part of paragraph beginning on Line 28 (Page 2) "Dr. Berman argues that the various departments within the Charleston textile mill do not differ significantly with regard to airborne fiber size based on his simulation study --- "in which the 83 samples were randomly regrouped into 10 new 'hypothetical' zones. This exercise is problematic for several reasons. First, it appears that the samples within these [zones of the SC plant] then new 'hypothetical zones' discussed by Dr. Berman were combined based on his fiber density method (described on pate 162)...."**

Actually, Kenny S. Crump, Dement, and I have had numerous conversations on this issue concerning the best manner for combining multiple TEM scans to derive size distributions and we are in the process of developing a joint manuscript that, among other things, addresses this issue. Both Dr. Crump and I believe that the "fiber density method" is the best method while Dr. Dement believes otherwise. The

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1 Note, I contacted NIOSH (the owner of the samples analyzed by Dement, Stayner, and coworkers) to request sections of the filters (or, at least, the prepared grids from a subset of the filters analyzed for the studies by Dement, Stayner, and coworkers) so that I could conduct more thorough analyses, but was told they were too valuable to distribute to outside parties. With this in mind, I have suggested to NIOSH that any future analyses of these and similar archived filters should be conducted in a sufficiently robust manner to support a broad range of studies by parties both in and outside of the agency and that interested parties be contacted to help design the analytical protocol prior to proceeding with such analyses. As stated in their Roadmap (NIOSH 2010), a broad view needs to be taken of such matters.

fiber density method is also consistent with what was recommended in Berman and Chatfield (1990), Chapter 7. One of the arguments I embrace supporting the "fiber density method" is that it is analogous to methods used for combining chemical analyses for samples with differing masses. To estimate the concentration of a constituent in a defined volume from samples with differing masses, the concentrations in each sample are weighted by the mass of the sample before averaging. This is based on the idea that the larger mass samples represent a larger fraction of the total mass so that they contribute more to the average. Similarly, filter samples that are more highly loaded represent a larger fraction of the air sampled than more sparsely loaded filters and should thus be weighted more heavily. Regardless, neither approach appears to be biased, so that differences in the means generated using either approach should ultimately be similar. In fact, other than achieving greater relative precision using the fiber density method, preliminary results from our joint study appear to indicate general comparability across the two approaches (Kenny S. Crump, Louisiana Tech University, personal communication). It may be that the difference in precision between the two approaches is because, under the fiber density method, the contribution that each fiber makes to a distribution is simply a function of its probability of being detected. Under the approach employed by Dement, Stayner, and coworkers (in contrast) the contribution of longer fibers are a function of the product of their individual probability of being detected in the long fiber scan and the overall probability of the longer scan size group of fibers being detected in the shorter-fiber scans. Thus, I do not agree that using the fiber density method in any way invalidates the findings in Berman (2010).

8. **Second part of paragraph beginning on Line 26 (Page 2): "....Secondly, Dr. Berman apparently combined all diameter categories within a give fiber length category in his analyses (page 176 and Table 7) and he used numerous tow [sic] sample Mann-Whitney tests for most of his analyses;..... a more appropriate statistical test to compare differences in bivariate size distributions across departments is a likelihood ratio chi-square based on a multinomial distribution.....".**

Contrary to this comment by Drs. Dement and Stayner, results of chi-square analyses that were applied to the data evaluated in Berman (2010) are presented or discussed in the text accompanying Table 2 and Figure 3. Results show that individual SC samples are highly significantly different from one another, as are samples of Grade 3 and (separately) Quebec Ore ($p<<0.0001$ between samples *within* in each group). Based on these results, applying chi-square analyses to compare results between these groups of samples (as opposed to between individual samples) would not be valid because the observed extra-Poisson variability (within groups) violates one of the underlying statistical requirements for chi-square analyses (Walters 2000, Kramer and Schmidhammer 1992). Bottom line: large, significant differences between samples within groups virtually guarantees a significant difference will be observed between groups, which renders the chi square test meaningless in such circumstances. Therefore, I disagree with the statement by Drs. Dement and Stayner that the "correct" way to compare the Grade 3 data (or ore data) with the SC data is to use a chi-square analysis.

9. **Paragraph beginning on Line 46 (Page 2): "A final argument against Dr. Berman's conclusions lies in the results of the analyses of lung cancer risk by TEM fiber size (Stayner et al, 2008). In these analyses, fiber size-specific exposure estimates were used in risk models....While all fiber size**

**categories were found to be significant predictors of risk, longer and thinner fibers were found to be stronger risk predictors. If Dr. Berman's conclusion that airborne fibers in textile operations are not different in size characteristics, use of our size-specific estimates should have simply introduced more noise and mask differences by fiber size....Similar results have now been obtained in studies of three asbestos textile plants in North Carolina (Dement et al., 2009, Loomis et al., 2009)."**

To reiterate (see Response No. 1 above), Berman (2010) does not conclude that there are no differences in fiber sizes between operations in the SC plant, only that any such differences are small relative to other sources of variation. Consequently, the findings of Stayner et al. (2008), Dement et al. (2009), and Loomis et al., (2009) are not inconsistent with the findings of Berman (2010). They simply suggest that whatever small differences exist in dust that may be explicitly attributable to differences in operations within zones of these plants, such differences may have differential health consequences that are sufficient to allow a well-designed study to tease out. However, it is also possible that the operations assigned the longest and thinnest categories in the studies by Dement, Loomis, Stayner, and coworkers happen to correlate with the operations in which the highest overall exposures also occur. Under such circumstances, the findings in these studies could simply be an artifact of such correlation that might nevertheless be consistent across the studies. In fact, as the cited studies state, the substantial correlation between fiber sizes observed across zones within each plant severely limits the power with which the effects of fiber size can be evaluated and interpreted with data from any of these studies (either from a single plant or from multiple plants within the same industry). This is also consistent with the findings of Berman and Crump (2008) that differences in fiber potency estimates observed between plants from the same industry (when fiber type is considered) are small relative to differences across industries. Clearly, studies of the effects of fiber size and type are best conducted by comparing observations across plants representing diverse industries (and exposure conditions) so that correlations between fiber sizes and types are unlikely to be important.

10. **Paragraph beginning on Line 4 (Page 3): "While Dr. Berman's Modified Elutriator Method offers a potentially useful tool for exploring relatively large differences in size distributions between industry sectors, this method cannot detect size differences within a give sector without additional considerations. Dr. Berman has not convincingly shown that airborne fiber sizes across textiles [sic] departments are the same and it is difficult to see how the current elutriator method could be used to study operations like friction or cement products where the raw asbestos fibers are incorporated into a solid matrix. In these industries dust characteristics in the initial mixing and blending operations of raw fiber would be expected to be different from those experienced in cutting, drilling, and sanding operations.....".**

Actually, I am currently preparing a manuscript documenting a study that examines differences in dust characteristics as a function of sanded and unsanded material. Thus, I suggest that, as long as the kinds of bulk materials examined are carefully and creatively chosen, the elutriator method may prove to be quite a powerful tool supporting elaboration of the effects of fiber size across most of the industries of potential interest. Again depending on bulk materials chosen, it may even be possible to examine whatever small differences may exist between operations within a textile plant, although the effects of fiber size are clearly easier to delineate by looking between industries.

11. **Paragraph beginning on Line 16 (Page 3): " We do not wish to convey the impression that Dr. Berman's elutriator method is without merit....However,, it is important that both strengths and weaknesses in this approach be recognized....".**

Ultimately, full reconstruction of historical exposures (and their validation) will likely require comparison across lung-tissue studies, archived air filter studies, and elutriator studies. Each offers unique advantages and limitations so that combining data acquired using the different approaches, especially where they can be compared from a common environment, should prove quite powerful.

**Declaration of Interest**

I consult for a variety of government and private organizations with competing interests, who (to the best of my knowledge) have no direct financial stake in the outcome of this research. As I have no financial stake in use of the elutriator method or its associated equipment, except for attracting additional research funding, I have no direct financial interest in the outcome of this research. Funding for all early work related to the subject matter of the Berman (2010) manuscript was provided by the U.S. Environmental Protection Agency (EPA). Funding provided for writing that manuscript (the subject of these responses) was provided as a grant by The National Stone, Sand, and Gravel Association (NSSGA), although they had no input into the preparation of that manuscript. The NSSGA neither funded nor had any other input into the writing of these responses. Financial support provided by the EPA and NSSGA should not be construed as an endorsement of the results of the previous analyses or the resulting manuscript (Berman 2010). The author has sole responsibility for the analyses, writing, and content of these responses.

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## TABLE 1: LENGTH AND WIDTH DISTRIBUTIONS DERIVED FROM DEMENT ET AL. 2008, TABLE 4

| | Prep | Carding | Ring Spinning | Mule Spinning | Foster Winding | Twisting | Universal Winding | Heavy Weaving | Light Weaving | Finishing | Min | Max | Mean | Max/Min Ratio | Ratio (Exclude Finishing) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Length | | | | | | | | | | | | | | | |
| <1.5 | 0.365 | 0.430 | 0.543 | 0.440 | 0.432 | 0.611 | 0.443 | 0.590 | 0.555 | 0.659 | 0.365 | 0.659 | 0.506 | 1.805 | 1.674 |
| 1.5-3 | 0.294 | 0.253 | 0.210 | 0.226 | 0.302 | 0.166 | 0.218 | 0.190 | 0.199 | 0.191 | 0.166 | 0.302 | 0.225 | 1.819 | 1.819 |
| 3-5 | 0.151 | 0.142 | 0.101 | 0.133 | 0.124 | 0.090 | 0.132 | 0.083 | 0.090 | 0.084 | 0.083 | 0.151 | 0.113 | 1.812 | 1.812 |
| 5-15 | 0.145 | 0.141 | 0.090 | 0.143 | 0.097 | 0.093 | 0.145 | 0.099 | 0.113 | 0.051 | 0.051 | 0.145 | 0.112 | 2.863 | 1.604 |
| 15-40 | 0.038 | 0.028 | 0.041 | 0.042 | 0.035 | 0.028 | 0.050 | 0.030 | 0.033 | 0.014 | 0.014 | 0.050 | 0.034 | 3.518 | 1.765 |
| >40 | 0.008 | 0.005 | 0.014 | 0.017 | 0.010 | 0.011 | 0.012 | 0.007 | 0.010 | 0.002 | 0.002 | 0.017 | 0.010 | 9.820 | 3.196 |
| Width | | | | | | | | | | | | | | | |
| <0.25 | 0.818 | 0.803 | 0.875 | 0.862 | 0.858 | 0.940 | 0.827 | 0.898 | 0.890 | 0.913 | 0.803 | 0.940 | 0.868 | 1.171 | 1.171 |
| 0.25-1 | 0.137 | 0.147 | 0.093 | 0.100 | 0.108 | 0.044 | 0.116 | 0.082 | 0.081 | 0.083 | 0.044 | 0.147 | 0.099 | 3.343 | 3.343 |
| 1-3 | 0.036 | 0.043 | 0.025 | 0.031 | 0.030 | 0.014 | 0.047 | 0.016 | 0.026 | 0.002 | 0.002 | 0.047 | 0.027 | 20.983 | 3.280 |
| >3 | 0.009 | 0.007 | 0.007 | 0.007 | 0.004 | 0.002 | 0.010 | 0.004 | 0.003 | 0.002 | 0.002 | 0.010 | 0.006 | 5.918 | 4.819 |

## TABLE 2: ANALYSIS OF SIZE DISTRIBUTIONS PRESENTED IN TABLE III OF LYNCH AND AYER (1966)

| | Plant | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Operation | A | B | C | D | E | F | G | H | I | All | Min | Max | Mean | SC Mean[a] |
| | Ratio of >5 to Total Fibers | | | | | | | | | | | | | |
| Fiber Prep | 0.39 | 0.81 | 0.57 | 0.54 | | 0.37 | 0.59 | 0.48 | 0.22 | 0.36 | 0.22 | 0.81 | 0.48 | 0.19 |
| Carding | 0.56 | 0.68 | 0.65 | 0.46 | | 0.58 | 0.47 | 0.48 | 0.24 | 0.47 | 0.24 | 0.68 | 0.51 | 0.18 |
| Spinning | 0.69 | 0.78 | 0.94 | 0.53 | | 0.69 | 0.44 | 0.50 | 0.24 | 0.50 | 0.24 | 0.94 | 0.59 | 0.17 |
| Twisting | 0.69 | 0.75 | 0.47 | 0.44 | | 0.69 | 0.50 | 0.43 | 0.35 | 0.48 | 0.35 | 0.75 | 0.53 | 0.13 |
| Winding | 0.64 | 0.89 | 0.93 | 0.61 | | 0.71 | 0.46 | 0.34 | 0.36 | 0.46 | 0.34 | 0.93 | 0.60 | 0.17 |
| Weaving | 0.62 | 0.44 | 0.79 | 0.53 | 0.81 | 0.76 | 0.60 | 0.37 | 0.52 | 0.45 | 0.37 | 0.81 | 0.59 | 0.15 |
| All | 0.49 | 0.74 | 0.60 | 0.35 | 0.87 | 0.65 | 0.50 | 0.44 | 0.29 | 0.45 | 0.29 | 0.87 | 0.54 | |
| | Ratio of >10 to Total Fibers | | | | | | | | | | | | | For >15[b] |
| Fiber Prep | 0.19 | 0.28 | 0.25 | 0.24 | | 0.14 | 0.26 | 0.26 | 0.10 | 0.20 | 0.10 | 0.28 | 0.21 | 0.046 |
| Carding | 0.24 | 0.30 | 0.29 | 0.26 | | 0.27 | 0.19 | 0.25 | 0.11 | 0.25 | 0.11 | 0.30 | 0.24 | 0.034 |
| Spinning | 0.33 | 0.46 | 0.32 | 0.35 | | 0.35 | 0.25 | 0.29 | 0.15 | 0.29 | 0.15 | 0.46 | 0.31 | 0.057 |
| Twisting | 0.40 | 0.48 | 0.30 | 0.37 | | 0.40 | 0.30 | 0.25 | 0.23 | 0.34 | 0.23 | 0.48 | 0.34 | 0.039 |
| Winding | 0.40 | 0.39 | 0.35 | 0.42 | | 0.44 | 0.28 | 0.20 | 0.25 | 0.34 | 0.20 | 0.44 | 0.34 | 0.053 |
| Weaving | 0.38 | 0.40 | 0.38 | 0.29 | 0.29 | 0.41 | 0.35 | 0.22 | 0.24 | 0.31 | 0.22 | 0.41 | 0.33 | 0.040 |
| All | 0.25 | 0.33 | 0.30 | 0.30 | 0.31 | 0.33 | 0.27 | 0.25 | 0.15 | 0.28 | 0.15 | 0.33 | 0.28 | |

**NOTES:**

[a] Derived from Dement et al. (2008) for the South Carolina Textile Plant

[b] For Ratio of >15 to Total Fibers